

CHLOROTHALONIL

APPENDIX I

PRODUCT FORMULATIONS CONTAINING MULTIPLE ACTIVE INGREDIENTS

The Agency does not routinely include, in its risk assessments, an evaluation of mixtures of active ingredients, either those mixtures of multiple active ingredients in product formulations or those in the applicator's tank. In the case of the product formulations of active ingredients (that is, a registered product containing more than one active ingredient), each active ingredient is subject to an individual risk assessment for regulatory decision regarding the active ingredient on a particular use site. If effects data are available for a formulated product containing more than one active ingredient, they may be used qualitatively or quantitatively^{1 2}.

Acute oral toxicity data (i.e., LD50 values) from mammalian studies for formulated products that contain chlorothalonil and one or more additional active ingredients are summarized below.

Currently, the Agency's guidance for assessing the potential risk of chemical mixtures is limited to human health applications (USEPA, 2000). However, the guidance includes principles for evaluating mixtures to assess potential interactive effects that are generally applicable. Consistent with EPA's Overview Document (USEPA 2004), the Agency's mixture guidance (USEPA 2000) discusses limitations in quantifying the risk of specified mixtures when there is differential degradation, transport and fate of chemical components following environmental release or application. The LD50 values are potentially useful only to the extent that a wild mammal would consume plants or animals immediately after these dietary items were directly sprayed by the product. Increasing time post application, the differential rates of degradation, transport, etc. for the active ingredients in the formulation only permit a qualitative discussion of potential acute risk (USEPA 2004).

As discussed in USEPA (2000) a quantitative component-based evaluation of mixture toxicity requires data of appropriate quality for each component of a mixture. In this mixture evaluation LD50s, with associated 95% confidence intervals, are needed for the formulated product. The same quality of data is also required for each component of the mixture. Given that many of the formulated products do not have LD50 values of the required quality and since LD50 values are not available for all the components of these formulations a quantitative analysis of potential interactive effects is not possible.

¹ Overview of the Ecological Risk Assessment Process in the Office of Pesticide Programs, Environmental Protection Agency (January 2004) (Overview Document).

² Memorandum to Office of Prevention, Pesticides and Toxic Substance, US EPA conveying an evaluation by the U.S. Fish and Wildlife Service and National Marine Fisheries Service of an approach to assessing the ecological risks of pesticide products (January 2004).

While a quantitative evaluation of the data is not possible with currently accepted scientific methods, as a screening tool, a qualitative analysis can be used to indicate if formulated products exhibit interactive effects (e.g., synergism or antagonism).

Of the 30 registered formulated products containing chlorothalonil, six products (EPA Reg. Nos. 100-1171, 100-1192, 1022-583, 1529-48, 55146-81 and 71711-2) have definitive LD50 values and associated confidence intervals for the product and formula components (excluding chlorothalonil).

For EPA Reg. No. 1022-583, the product LD50 value can be attributed solely to the toxicity of the methylenebis thiocyanate. When this product LD50 (353 mg/kg) and its associated confidence interval (247-506 mg/kg) are adjusted for the percent methylenebis thiocyanate (14.7%), the adjusted LD50 value of 51.9 mg/kg (CI range of 36.3-74.4 mg/kg) is not statistically distinct from the LD50 of methylenebis thiocyanate (68.3 mg/kg, CI range 49.4-94.3 mg/kg). Similarly, for EPA Reg. No. 55146-81, the toxicity can be attributed to the active ingredient mefenoxam. When the LD50 for this product (5041 mg/kg) and its confidence interval (4334-5863 mg/kg) are adjusted for percent mefenoxam (4.4%), the adjusted LD50 value of 222 mg/kg (CI: 191-258 mg/kg) is within a factor of two of the confidence interval for mefenoxam (490 mg/kg; CI: 360-666 mg/kg) and the difference is not considered to be toxicologically significant.

While there is no confidence interval associated with the LD50 (>10,000 mg/kg) for chlorothalonil, a review of the LD50 values for the remaining four products (EPA Reg. Nos. 100-1171, 100-1192, 1529-48 and 71711-2), show greater product toxicity (lower LD50 values) than expected, based on the LD50 values and proportion (percentage) of the product components. In these four cases, the product LD50 values are lower than the LD50 values for each component in the formulation. Although the active ingredients are not expected to have similar mechanisms of action, metabolites, or toxicokinetic behavior, based on these evaluations of the best available data and the Agency's existing guidance, it is not possible to conclude that these formulations reflect an independent additive toxicity response and not an interactive effect.

Pesticide Products Formulated with Chlorothalonil and Other Pesticide Active Ingredients

CHLOROTHALONIL PRODUCTS^{3 4}

PRODUCT/TRADE NAME	EPA Reg.No.	% Chlorothalonil	PRODUCT		ADJUSTED FOR ACTIVE INGREDIENT	
			LD 50 (mg/kg)	CI (mg/kg)	A.I Adjusted CI (mg/kg)	A.I Adjusted LD50 (mg/kg)
Mefenoxam/Bravo	100-800	72	>500	No Data	No Data	No Data
Quadris Opti	100-1171	46	1750	732-4440	805	337-2042
Tilt Bravo SE	100-1192	38.5	3129	1750-5000	1205	674-1925
Ridomil Gold Bravo SC	100-1221	33.1	>5000	NA Limit Dose	No Data	No Data
Instrata	100-1231	29.9	>1750	No Data	No Data	No Data
Riverdale CTM Fungicide	228-390	72	No Data	No Data	No Data	No Data
Banol C	432-961	30.5	>2000	No Data	No Data	No Data
Cuprinol Stain and Wood Preservative	577-544	0.7	No Data	No Data	No Data	No Data
Spectro 90 WDG	1001-72	72	>500	No Data	No Data	No Data

³ From registrant submitted data to support registration. Compiled by Office of Pesticide Programs Health Effects Division.

⁴ Chlorothalonil LD50: >10, 000 mg/kg; CI: N/A

PRODUCT/TRADE NAME	EPA Reg.No.	% Chlorothalonil	PRODUCT		ADJUSTED FOR ACTIVE INGREDIENT	
			LD 50 (mg/kg)	CI (mg/kg)	A.I Adjusted CI (mg/kg)	A.I Adjusted LD50 (mg/kg)
NeXgen	1022-583	14.5	353	247-506	51	36-73
Densil CA	1258-1270	47	>500	No Data	No Data	No Data
Fungitrol 2010	1529-47	20.06	2407	689-8403	483	138-1686
Fungitrol 2002	1529-48	48	1897	1630-2208	911	782-1060
Helena Bravo S	5905-472	19.15	>5020	NA Limit Dose	NA Limit Dose	NA Limit Dose
The Anderson 3-Way Snowmold Fungicide	9198-227	3.9	5000	NA Limit Dose	NA Limit Dose	NA Limit Dose
Terranil S	9779-337	19.15	>5000	NA Limit Dose	NA Limit Dose	NA Limit Dose
Terranil CU	9779-339	24	1500	1130-1991	360	271-478
Lesco TwoSome Flowable Fungicide	10404-60	40	4670	No Data	No Data	No Data
Consyst WDG	48234-7	50	>6300	No Data	No Data	No Data
Flouronil Fungicide	55146-81	72	5041	4334-5863	3629	3120-4221
ECHO Home Garden Fungicide and Insecticide	60063-15	3.75				
Acticide PM	67071-2	14.7	>5000	NA Limit Dose	NA Limit Dose	NA Limit Dose

PRODUCT/TRADE NAME	EPA Reg.No.	% Chlorothalonil	PRODUCT		ADJUSTED FOR ACTIVE INGREDIENT	
			LD 50 (mg/kg)	CI (mg/kg)	A.I Adjusted CI (mg/kg)	A.I Adjusted LD50 (mg/kg)
Acticide PM Flowable	67071-15	14.7	>5000	NA Limit Dose	NA Limit Dose	NA Limit Dose
Acticide SR-1216/6	67071-17	8.8	1310	1011-1698	115	89-149
THOR GMBH Acticide PAX	67071-39	11.8	No Data	No Data	No Data	No Data
Moncut CL Flowable	71711-2	38.6	1570	1140-2410	606	440-930
NAI-301 4 SE Fungicide	71711-24	21.65	>5000	NA Limit Dose	NA Limit Dose	NA Limit Dose
Intace Fungicide B-6773	74075-1	28.3	>2000	No Data	No Data	No Data
TM + CTN E-Pro 66.6 WDG Fungicide	79676-27	50	No Data	No Data	No Data	No Data
TM + CTN E-Pro WDG Fungicide	79676-28	72	>500	No Data	No Data	No Data
Peregrine	81943-7	50	No Data	No Data	No Data	No Data